REMARKS

Rejection of Claims 1-9 Under 35 U.S.C. §112, first paragraph

Claims 1-13 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking written description. Applicants respectfully traverse the rejection.

The Office Action asserts that "there is nothing on the record to show that the specification is enabled for the full scope of the claims and therefore does not meet the written description requirement." *See* page 4, third full paragraph. The Office appears to confuse the standards for written description and enablement. The written description and enablement requirements of the first paragraph of 35 U.S.C. §112 are separate and distinct requirements and each have their own standard. *See e.g., Vas-Cath Inc. v. Mahurkar,* 19 USPQ2d 1111, 118 (Fed. Cir 1991). The Office Action also asserts that no structural description of the claimed variants is provided. This is not the standard for written description. Rather, the standard for written description requires that one of skill in the art must recognize that the applicant was in possession of the claimed genus, that is, variants of SEQ ID NO:2. Importantly:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2001) (citations omitted).

Satisfactory disclosure of a representative number of species depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common

attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. One species can adequately support a genus.

What is a representative number of species depends on whether one of skill in the art would recognize that the Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed or claimed. Distinguishing characteristic such as:

A. partial structure;

B. physical and/or chemical properties;

C. functional characteristics;

D. known or disclosed correlation between structure and function;

E. method of making; and

F. combinations of A-E

should be considered. All of these factors, in view of the level of skill and knowledge in the art in light of and consistent with the written description, should be considered. See M.P.E.P. § 2163.

In the instant case, the partial structure of claimed variants are known, *i.e.*, sequences that having at least 85% identity to SEQ ID NO:2. Therefore, the variants have about 17 amino acids in common with the 20 amino acid long SEQ ID NO:2. The specification also discloses 7 related sequences that are useful in the invention. See specification, page 6. These 7 sequences can be considered variants of each other. When the sequence of SEQ ID NO:2 is compared to the sequences of SEQ ID NOs:1, and 3-7, highly conserved amino acids and partially conserved

amino acids are revealed. See Table 1, attached. Table 1 demonstrates that positions 3, 8, and 13 of SEQ ID NO:2 are highly conserved across the seven sequences (see Table 1, dark gray columns). Additionally, positions 1, 4, 5, 6, 7, 9, 10, 11, 12, and 15 are partially conserved across the 7 sequences (see Table 1, light gray columns). That is, only 2 different amino acids appear in these positions. For instance, only K or N appear as amino acids in position 1 across the seven sequences. One of skill in the art would recognize that variants should likely retain the amino acids at positions 3, 8, and 13 and that one of two amino acids should likely be present at positions 1, 4, 5, 6, 7, 9, 10, 11, 12, and 15. One of skill in the art would also recognize that amino acids at position 2, 14, and 16-20 could tolerate a greater range of amino acid substitutions. Therefore, the specification provides structural guidance for the claimed variants.

Furthermore, the physical properties and functional characteristics of the variants are disclosed in the instant specification. That is, the specification teaches that the variants specifically bind to an anti-*Ehrlichia* antibody and also teaches how to test if such variants specifically bind to an anti-*Ehrlichia* antibody. *See* specification page 10, line 6 through page 11, line 6; page 11, line 21- page 16, line 8; Example 1. Methods of making the variants of SEQ ID NO:2 are well-known in the art and are described in the specification. *See e.g.* page 5, lines 7-14; page 6, line 3 through page 7, line 5; page 7, line 12 through page 9, line 7; page 18, line 19 through page 19, line 13; page 7, line 6 through page 9, line 7. One of skill in the art could make and test variants of invention given the specification and the knowledge in the art.

Therefore, one of skill in the art would recognize that applicant was in possession of the necessary common attributes of features of the elements possessed by the members of the genus in view of the species disclosed because the partial structure, physical and/or chemical properties, functional characteristics, and methods of making the claimed variants is disclosed in

the specification. The written description does not have to be of such specificity that it would provide individual support for each species that the genus embraces.

Therefore, when all factors are considered, one of skill in the art would recognize from the disclosure that the Applicants were in possession of the claimed invention. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-13 Under 35 U.S.C. §112, first paragraph

Claims 1-13 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Applicants respectfully traverse the rejection.

The Office Action alleges that under the enablement requirement a structural description of the claimed variants must appear in the specification and alleges that no such description is provided by the specification.

However, a structural description of the claimed variants is indeed provided by the specification. The variants are phenotypically silent or conservative amino acid substitution variants that have at least 85% identity to SEQ ID NO:2, and specifically bind to an anti-*Ehrlichia* antibody. Since SEQ ID NO:2 is about 20 amino acids long, an amino acid substitution variant has only about 3 amino acid substitutions at the most. The specification also discloses 7 related sequences that are useful in the invention. See specification, page 6. These 7 sequences can be considered variants of each other. When the sequence of SEQ ID NO:2 is compared to the sequences of SEQ ID NOs:1, and 3-7, highly conserved amino acids and partially conserved amino acids are revealed. See Table 1, attached. Table 1 demonstrates that positions 3, 8, and 13 of SEQ ID NO:1 are highly conserved across the seven sequences (see Table 1, dark gray columns). Additionally, positions 1, 4, 5, 6, 7, 9, 10, 11, 12, and 15 are partially conserved across the 7 sequences (see Table 1, light gray columns). That is, only 2

different amino acids appear in these positions. For instance, only K or N appear as amino acids in position 1 across the seven sequences (see Table 1). One of skill in the art would recognize that the claimed variants should likely retain the amino acids at positions 3, 8, and 13 and that one of two amino acids should likely be present at positions 1, 4, 5, 6, 7, 9, 10, 11, 12, and 15. One of skill in the art would also recognize that amino acids at positions 2, 14, and 16-20 could tolerate a greater range of amino acid substitutions. Therefore, the specification provides structural guidance as to which amino acids can be changed so that the variant polypeptides retain their biological function.

Applicants remind the Office that the standard for enablement is whether one reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the patent coupled with information known in the art (3) without undue experimentation. As taught in the specification and described above, one of skill in the art could make the claimed variants while maintaining binding to an anti-*Ehrlichia* antibody, without undue experimentation. *See e.g.*, specification at page 5, line 6 through page 11, line 20. Therefore, the claims are enabled. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-13 Under 35 U.S.C. §102(a)

Claims 1-13 stand rejected under 35 U.S.C. §102(a) as allegedly anticipated by Rikihisa *et al.* Applicants respectfully traverse the rejection.

The Office Action asserts that the claims are drawn to compositions and articles of manufacture consisting essentially of an isolated polypeptide shown in SEQ ID NO:2 or an phenotypically silent amino acid substitution variant, or a conservative amino acid substitution variant thereof. The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel

characteristic(s) of the claimed invention." *See, In re Herz*, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original); MPEP §2111.03.

The claims recite an *E. canis* polypeptide fragment. The polypeptide fragments are useful, *inter alia*, to detect the presence of anti-*Ehrlichia* antibodies. The polypeptide fragments can be used as reagents in assays that provide greater sensitivity than the reagents taught in Rikihisa (*i.e.*, whole, recombinant proteins). See declaration of Dr. Chandrashekar, paragraphs 2-3 and 6-7 (of record). The specification also teaches that:

> currently known assays for detecting anti-*Ehrlichia* antibodies or fragments thereof are severely limited in usefulness because of sensitivity and specificity issues directly related to the impure nature of the *Ehrlichia* antigen used in these tests. See page 2, line 25 through page 3, line 1.

The Office appears to assert that the full-length proteins taught by Rikihisa would read on claimed polypeptide fragments. However, the addition of amino acids to the polypeptides so they encompass the whole proteins of Rikihisa would materially affect the basic and novel characteristics of the polypeptides. That is, use of full-length proteins would result in assays that are less sensitive than those disclosed in the instant specification. As such, the claims cannot be read so that the whole proteins of the prior art read on the claimed fragments.

Rikihisa does not anticipate claims 1-13 because Rikihisa does not teach, suggest, or inherently disclose each and every element of claims 1-13. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-9 Under 35 U.S.C. §112, second paragraph

Claims 1-9 stand rejected under 35 U.S.C. §112, second paragraph as allegedly lacking definiteness. Applicants respectfully traverse the rejection.

The Office Action asserts that claims 1-9 are indefinite for the use of the term "phenotypically silent amino acid substitution variants." Initially, claims 7, 8 and 9 do not contain this term. As such, the rejection is improper for these claims.

The Office Action asserts that the metes and bounds of "phenotypically silent amino acid substitutions" cannot be ascertained by what is disclosed in the specification. However, the test for definiteness is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). One of skill in the art would understand the meaning of phenotypically silent amino acid substitution variants given the specification. The specification teaches phenotypically silent amino acid substitution variants and how to identify such variants at, *inter alia*, page 7, line 10 through page 9, line 7. In particular, the specification teaches that a phenotypically silent amino acid substitution has little effect on activity of a variant polypeptide fragment. One of skill in the art would understand, in light of the specification and the state of the art, that variants of SEQ ID NO:2 that have about the same biological activity of a polypeptide of SEQ ID NO:2 are encompassed by "phenotypically silent amino acid variants".

The claims are therefore definite and applicants respectfully request withdrawal of the rejection.

Conclusion

Applicants respectfully submit that the claims are in a condition for allowance. If the Examiner is of the opinion that that a telephone conference would expedite the prosecution of the application, the Examiner is encouraged to contact Applicants undersigned representative.

Respectfully submitted,

Date: 7-13-04 by: _____

Lisa M.W. Hillman
Reg. No. 43,673